

Application No. 10/814,025

Second Preliminary Amendment of June 3, 2004

**Amendments to the Claims**

This listing of claims will replace all prior versions, and listing of claims in the application:

**Listing of Claims**

- 1- 47. (Canceled)
48. (New) A method for producing glucocerebrosidase useful for the treatment of a human patient having Gaucher's disease comprising the steps of:
- a. providing a culture of mammalian cells capable of expressing glucocerebrosidase;
  - b. treating said cells with an inhibitor of carbohydrate processing that acts to inhibit the conversion of  $\text{Glc}_3\text{Man}_9\text{GlcNac}_2$  to smaller species; and
  - c. recovering glucocerebrosidase from said culture,
- wherein said recovered glucocerebrosidase contains a higher number of exposed mannose residues than does human placental glucocerebrosidase.
49. (New) The method of claim 48, wherein said inhibitor is deoxy-mannojirimycin.
50. (New) The method of claim 48, wherein said inhibitor is swainsonine.
51. (New) The method of claim 48, wherein said inhibitor is castanospermine.
52. (New) The method of claim 48, wherein said inhibitor is deoxy-nojirimycin.
53. (New) The method of claim 48, wherein said inhibitor is N-methyl-deoxy-nojirimycin.
54. (New) A method of increasing the number of exposed mannose residues on glucocerebrosidase comprising treating a culture of mammalian cells expressing glucocerebrosidase with an inhibitor of carbohydrate processing that acts to inhibit the conversion of  $\text{Glc}_3\text{Man}_9\text{GlcNac}_2$  to smaller species.
55. (New) The method of claim 54, wherein said inhibitor is deoxy-mannojirimycin.
56. (New) The method of claim 54, wherein said inhibitor is swainsonine.
57. (New) The method of claim 54, wherein said inhibitor is castanospermine.
58. (New) The method of claim 54, wherein said inhibitor is deoxy-nojirimycin.
59. (New) The method of claim 54, wherein said inhibitor is N-methyl-deoxy-nojirimycin.

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60. (New) A composition comprising glucocerebrosidase produced according to the method of claim 54.
61. (New) A pharmaceutical composition useful for the treatment of a human patient having Gaucher's disease comprising glucocerebrosidase containing a higher number of exposed mannose residues than human placental glucocerebrosidase, wherein said glucocerebrosidase is produced by treating cells expressing glucocerebrosidase with an inhibitor of carbohydrate processing that acts to inhibit the conversion of  $\text{Glc}_3\text{Man}_9\text{GlcNac}_2$  to smaller species.
62. (New) The pharmaceutical composition of claim 61, wherein said inhibitor is deoxy-mannojirimycin.
63. (New) The pharmaceutical composition of claim 61, wherein said inhibitor is swainsonine.
64. (New) The pharmaceutical composition of claim 61, wherein said inhibitor is castanospermine.
65. (New) The pharmaceutical composition of claim 61, wherein said inhibitor is deoxy-nojirimycin.
66. (New) The pharmaceutical composition of claim 61, wherein said inhibitor is N-methyl-deoxy-nojirimycin.
67. (New) A method of treating a human patient having Gaucher's disease comprising administering to said patient the composition of claim 61 in an amount sufficient to alleviate the clinical symptoms of Gaucher's disease.
68. (New) A method of treating a human patient having Gaucher's disease comprising administering to said patient the composition of claim 62 in an amount sufficient to alleviate the clinical symptoms of Gaucher's disease.
69. (New) A method of treating a human patient having Gaucher's disease comprising administering to said patient the composition of claim 63 in an amount sufficient to alleviate the clinical symptoms of Gaucher's disease.
70. (New) A method of treating a human patient having Gaucher's disease comprising administering to said patient the composition of claim 64 in an amount sufficient to alleviate the clinical symptoms of Gaucher's disease.

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71. (New) A method of treating a human patient having Gaucher's disease comprising administering to said patient the composition of claim 65 in an amount sufficient to alleviate the clinical symptoms of Gaucher's disease.
72. (New) A method of treating a human patient having Gaucher's disease comprising administering to said patient the composition of claim 66 in an amount sufficient to alleviate the clinical symptoms of Gaucher's disease.